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EXAMINER	
LAM, ANN Y	
ART UNIT	**PAPER NUMBER**
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,493	RICH ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *36-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-53* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/24/04*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20060528* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-35, drawn to a method for creating a profile of interactions, classified in class 435, subclass 7.1.

II. Claims 36-53, drawn to a kit, classified in class 436, subclass 518.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another and materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the apparatus as claimed can be used to practice another and materially different process because the apparatus can be used for purification or for synthesis of molecules rather than for creating a profile of interactions.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

During a telephone conversation with Kenneth Weber on April 7, 2006 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-35. Affirmation of this election must be made by applicant in replying to this Office action. Claims 36-53 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Drawings

The drawings are objected to because the figure labeled "I5I-a" should be –5a--. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the

remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities: the brief description of the drawings do not describe figures 4a, 4b, 4c, 5a, 5b, 5c, 6a, 6b, 6c, 7a, 7b,7c, 8a, 8b, 8c, 9a, 9b nor 9c. The description of "Figure 4" for example is insufficient to describe figures 4a, 4b and 4c.

Appropriate correction is required.

Claim Objections

Claim 35 is objected to because of the following informalities: a period is missing. Appropriate correction is required.

Claims 16, 26, 32 are objected to because of the following informalities: --further—should be inserted before "comprising" in line 1 of the claims respectively. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, lines 1-2, recites "creating a profile of interactions between components of at least one multicomponent biological complex for a sample", which suggests that the complex is a separate element from the sample. However, claim 1, lines 4-5, recites "the aliquot comprises the multicomponent biological complex from the sample", which suggests that the sample comprises the complex. Thus, it is not clear whether the complex is interacting with the sample or whether the sample comprises the complex. It appears that Applicant intends for the sample to be comprised of the complex and thus will be interpreted so for purposes of examination.

Claim 1, line 11, recites "the successive elution washes". The claim lacks antecedent basis for this limitation.

Claim 1, line 9, recites "the concentration". The claim lacks antecedent basis for this limitation.

Claim 1, line 12, recites "the measurements". The claim lacks antecedent basis for this limitation.

Claim 1, line 12, recites "a complex". It appears that Applicant intends to refer to the complex in line 2, and will be interpreted so for purposes of examination. However this is not clear in the claims and clarification is requested.

Claim 1, line 8, recites "the immobilized complex". The claim lacks antecedent basis for this limitation. It appears that Applicant intends to refer to the complex in line 5. However this is not clear and should be clarified.

Claim 1, line 12, recites "a sample". It appears that Applicant intends to refer to the sample in line 2, and will be interpreted so for purposes of examination. However this is not clear in the claims and clarification is requested.

Claim 1, line 6, recites a first component, and line 11, recites measuring a second component in the successive elution washes, and line 12-13 recites "whereby the profile for a complex from a sample comprises the measurements from the elution washes". However, only one measurement has been recited, i.e., in line 11. There should be more than one measuring step in order for there to be measurements (i.e., in the plurality), however this is not recited and clarification is requested. For purposes of examination, the claim will be interpreted as if there are more than one measuring step.

Likewise, independent claim 22, line 18, and independent claim 28, line 14, claim 31, line 20, each recite "measurements" but has only one step of measuring. There should be more than one measuring step in order for there to be measurements (i.e., in the plurality), however this is not recited and clarification is requested. For purposes of examination, the claim will be interpreted as if there are more than one measuring step.

Claim 2, line 1, recites "the samples". It appears that Applicant intends to refer to the sample (singular form) in line 2, and will be interpreted so for purposes of examination. However this is not clear in the claims and clarification is requested.

Claim 2, lines 1-2, recites "the group". The claim lacks antecedent basis for this limitation.

Claim 13, line 2, recites "the biospecific capture reagent". The claim lacks antecedent basis for this limitation. For examination purposes, the Office will interpret the biospecific capture reagent to be referring to the biospecific affinity molecule in claim 1, line 6.

Claim 16, line 1, recites "the immobilized complex. The claim lacks antecedent basis for this limitation. It appears that Applicant intends to refer to the complex in claim 1, line 8, (which itself lacks an antecedent basis in the claim, as discussed above) and will be interpreted so for purposes of examination. Applicant should set forth an antecedent basis for "the immobilized complex".

Claim 21, line 3, recites "whereby the profile further comprises the measurements of the complex". It appears that the measurements in claim 21, line 3, is referring to the measurements from the elution washes in claim 1, line 11. However, claim 1 (from which claim 21 depends) already recites in line 12-13, "whereby the profile for a complex from a sample comprises the measurements from the elution washes". Thus it is not clear what measurement is being made in claim 21, line 3. For purposes of examination, the Office will interpret claim 21, line 3 to be referring to the same measurement as in claim 1, line 11.

Claim 22, lines 7, 8, and 20 recite "the sample". It appears that Applicant intends to recite --each sample in the set--, rather than just a sample from one of the subset of

samples, and will be interpreted so for purposes of examination. However, this is not clear in the claims and clarification is requested.

Claim 24, line 2, recites "the inhibitory RNA". The claim lacks antecedent basis for this limitation. For purposes of examination, the Office will interpret the limitation to mean inhibitor RNA.

Claim 24, recites "wherein the different biological characteristics are exposure to an inhibitor RNA or non-exposure to the inhibitory RNA." It is not clear as to what is being claimed because a biological characteristic of a subset of a sample appears to suggest a property of the subset but claim 24 suggests that the characteristics is not a property but is the condition of exposure or non-exposure to an inhibitor RNA. Because of the ambiguity in the claim, the claim is interpreted to mean that the subset is either inhibited by an inhibitor, i.e., salt in the gradient of salt concentration, or it is not

Claim 26, line 2, recites "the sample". It appears that Applicant intends to recite --each sample in the set--, rather than just a sample from one of the subset of samples, and will be interpreted so for purposes of examination. However, this is not clear in the claims and clarification is requested.

Claim 31, line 7, recites "the sample". It appears that Applicant intends to recite --each sample in the set--, rather than just a sample from one of the subset of samples, and will be interpreted so for purposes of examination. However, this is not clear in the claims and clarification is requested.

Claim 31, line 19, recites "a sample". It appears that Applicant intends to refer to the set of biological samples in line 2. However this is not clear and clarification is requested.

Claim 34, lines 2, and claim 35, lines 1-2, both recite "the samples". It appears that Applicant intends to refer to the set of biological samples in claim 31, line 2. However, this is not clear and clarification is requested.

Claim 35 does not make sense because it is an incomplete sentence. (There is no period and no verb.) For purposes of examination, the Office will interpret the claim as if "to detect" in line 2 is –detects--.

The remaining claims are rejected under 112, second paragraph because they depend from a claim (1, 22, 28 or 31) that is vague and indefinite for the reasons given above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1-6, 8, 11, 12, 14-15 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Church et al., 6,548,021.

As to claims 1 and 28, Applicant claims a method for creating a profile of interactions between components of at least one multicomponent biological complex for a sample which is taught by Church et al. because Church et al. teach assaying for the relative affinities for the recognition sites for a protein by binding them to chips or chromatography supports to which are complexed oligonucleotides and eluting them off in buffers of gradually increasing ionic strength (see col. 23, lines 46-53).

As to the claimed step (a), i.e., providing an aliquot from the sample, wherein the aliquot comprises the multicomponent biological complex from the sample immobilized on a solid support through a biospecific affinity molecule, wherein the affinity molecule binds a first component of the complex and wherein unbound material has been removed from the solid support, this is disclosed by Church et al. because Church et al. teach incubating a plurality of protein molecules with an array of nucleic acids under conditions which permit protein:nucleic acid binding (col. 23, lines 27-29).

As to the claimed step (b), i.e., washing the immobilized complex with a first sequence of elution washes, wherein the concentrations of a first solute in each elution wash in the sequence form a gradient of increasing or decreasing concentration, this is disclosed by Church et al. because Church et al. teach eluting off the proteins in buffers of gradually increasing ionic strength (see col. 23, lines 46-53).

As to the claimed step (c), i.e., measuring a second component in the successive elution washes; whereby the profile for a complex from a sample comprises the measurements from the elution washes, this is disclosed by Church et al. because Church et al. teach assaying the bound proteins by eluting them off in buffers of

gradually increasing ionic strength and that the binding affinity is directly proportional to the salt concentration required to remove a given protein from a nucleic acid molecule (col. 23, lines 46-54).

As to claim 2, the samples are from cell extracts (col. 26, line 44).

As to claim 3, the at least one complex is one complex (i.e., protein, col. 23, lines 46-53).

As to claim 4, the at least one complex is a plurality of complexes, each bound through a biospecific affinity reagent (i.e., proteins, col. 23, lines 46-53).

As to claim 5, the affinity molecule is nucleic acid (col. 23, line 49).

As to claim 6, the affinity molecule is immobilized to the solid support before binding the complex (col. 23, lines 18-19 and lines 48-50).

As to claim 8, the solid support is a chromatographic resin (col. 23, line 48).

As to claims 11 and 12, the washes are performed in a flow-through column (col. 23, line 48).

As to claim 14, the unbound material is removed with an initial wash (col. 23, line 51).

As to claim 15, the solute is an ion or salt (see col. 23, line 52 and 60).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 9, 10, 16-19, 21-27 and 29-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Church et al., 6,548,021

Church et al. disclose the invention substantially as claimed (see above with respect to claim 1). More specifically, Church et al. teach that an array of nucleic acid sequences immobilized on a support, such as chips or chromatography supports, can be used for binding to proteins for which it has affinity and for subsequently eluting off the proteins in buffers of gradually increasing ionic strength to determine binding affinity, which is directly proportional to the salt concentration required to remove a given protein form a nucleic acid molecule (col. 23, lines 48-51).

As to claims 9 and 10, while Church et al. discloses chips and chromatography supports as examples of the solid support for this assay, Church et al. do not specifically teach that the elution washes may be performed in a non-flow-through device such as a closed bottomed microtiter plate (as claimed by Applicant in claims 9 and 10).

However Church et al. do disclose that solid supports of the invention may be pins that are inserted into containers in a tray such as 96-well microtitre dish (col. 17, line 62 – col. 18, line 4). While Church et al. do not specifically disclose that such solid supports in a microtitre well may be utilized for the assay involving elution washes to determine binding affinity, it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize such a solid support for the assay because Church et al. teach use of the solid supports in general for the elution washes and

Church et al. also teach that a pin in a microtitre well is another example of a solid support that is useful for the disclosed inventions.

As to claims 17-19 and 21, while Church et al. teach use of mass spectrometry to identify the proteins (col. 23, lines 41-44) before the assay with the elution washes are performed (col. 23, lines 46-41), and that the binding affinity is directly proportional to the salt concentration required to remove a given protein from a nucleic acid molecule (col. 23, lines 52-54), Church et al. do not specifically disclose how the removal of the protein is detected. However, Church et al. teach mass spectrometry for detection of the proteins (prior to the assay with the elution washes), and thus it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize mass spectrometry to detect the protein, or its removal or absence, from the solid support after the elution washes because Church et al. teach this as a particular method of detection of molecules. It would have been obvious to one of ordinary skill in the art from the disclosure of Church et al. that the detection of the protein that remains on the solid support or its removal or absence from the solid support in the elution washes requires a detection step and that such detection may be the mass spectrometry disclosed by Church et al. for the detection of proteins. Moreover, Church et al. on column 27, lines 59-62, disclose that relative binding efficiencies are determined by a method similar to the assay using buffers of graded salt concentrations, wherein the method utilizes labels and that the proteins are detected on the solid support to determine the binding efficiencies, i.e., whether or not they remain bound (col. 27, lines 50-61). Thus, this also suggests that a detection of bound proteins must be made in the

assay utilizing buffers of graded salt concentrations in order to determine relative binding efficiencies or affinities.

Thus, as to claims 21, 25, 29, and 33, the step of measuring the components of the complex still immobilized is suggested by Church et al. (col. 23, lines 52-53). As to claim 17, the limitation reciting that the second component may be detected by an optical method is suggested by Church et al. (col. 23, lines 42-44). As to claims 18 and 19, the limitation reciting that the second component is detected by mass spectrometry is suggested by Church et al.(col. 23, lines 42-44).

As to independent claims 22, 31, and 35, Applicant claims the step of providing two set of biological samples, each subset characterized by a different biological characteristic and creating a profile of interactions for each sample by washing an immobilized complex with a plurality of successive elution washes wherein concentrations of a solute in each successive elution washes form a gradient of increasing or decreasing concentration and measuring a second component in the successive elution washes and comparing the profiles from the samples to detect differences in interaction between components in each subset. This is substantially disclosed by Church et al. because Church et al. teach assaying for the relative affinities for the recognition sites for a protein by binding them to chips or chromatography supports to which are complexed oligonucleotides and eluting them off in buffers of gradually increasing ionic strength, or salt concentrations (see col. 23, lines 46-61).

However, Church et al. do not teach that the subsets of the set of biological samples each are characterized by a different biological characteristic. Also, while

Church et al. teach detecting relative affinities of a nucleic acid molecule for proteins to which it binds (col. 23, lines 46-47), Church et al. do not explicitly disclose comparing the profiles from the different subsets of a sample to detect differences in interaction between components in each subset.

Church et al. however suggests comparing different subsets of a sample because the disclosure of detecting relative affinities of a nucleic acid molecule for proteins to which it binds (col. 23, lines 46-47) suggests a comparison between different proteins for their affinity to a nucleic acid molecule. Moreover Church et al. teach another assay embodiment using labels for the determination of relative binding efficiencies of a protein to a nucleic acid molecule rather than using buffers of graded salt concentration. Church et al. teach in this disclosure that comparative quantitation of the binding efficiencies of different proteins to features on the array may be made if so desired (col. 27, lines 59-61). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the assay using buffers of graded salt concentration for comparison between two proteins because Church et al. teach it may be desirable to compare binding affinities between different proteins. (The two different proteins are considered to be the same as the subsets of a sample, as claimed by Applicant.)

As to claim 23 (dependent from claim 22), Applicant claims that the different biological characteristics are pathological versus non-pathological or drug responder versus drug non-responder. This is disclosed by Church et al. because Church et al. teach that the invention is useful for assaying protein/nucleic acid interactions where the

protein or the nucleic acid sequence or both have been mutated, and that the arrays of the invention are useful for identifying compositions that are of potential scientific or clinical interest, particularly those with therapeutic potential (col. 28, lines 41-45 and 56-59).

As to claim 24 (dependent from claim 22), Applicant claims that the different biological characteristics are exposure to an inhibitor RNA or non-exposure to the inhibitory RNA. This is disclosed by Church et al. because Church et al. teach that the nucleic acid may be RNA, and the salt is considered an inhibitor (see for example, col. 24, lines 60-62). Because of the ambiguity in the claim, as indicated above, the claim is interpreted to mean that the subset is either inhibited by an inhibitor, i.e., salt in the gradient of salt concentration, or it is not. Because assays for a comparison of different proteins as suggested by Church et al., as described above, involve different proteins, it would have been obvious that proteins that are eluted at different salt, i.e., inhibitor, concentrations have different characteristics, i.e., have different binding affinities.

As to claim 16 (dependent from claim 1), and claim 26 (dependent from claim 22), claim 30 (dependent from claim 28), and claims 32 and 34 (both dependent from claim 31), Applicant claims the steps of further performing the successive elution washes with elution washes comprising a different type of solute than the first solute. While this is not disclosed by Church et al., Church et al. teach the motivation to perform such steps. Church et al. teach utilizing buffers of gradually increasing ionic strength to determine binding affinity (col. 23, lines 51-52), and disclose that the solute is a salt (col. 23, line 60). Church et al. also teach that in addition to changes in salt

concentration in an in vitro system, it is desirable to examine factors which might in a living system influence or be made to influence nucleic acid/protein interactions (col. 23, lines 60-64). Church et al. teach that this method is applicable if it is advantageous to inhibit binding of a protein to a particular recognition site for a protein in order to nullify its influence of a given gene (col. 23, lines 64-67). Church et al. teach that inhibitors may be salts, enzymes and other proteins (col. 24, lines 61-63). Thus Church et al. suggest that enzymes and other proteins may be inhibitors as well as salts. It would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the assay using inhibitors other than salts in a gradient of concentrations because Church et al. teaches that enzymes and other proteins may be inhibitors as well as salts. One of ordinary skill in the art would recognize that assaying with different inhibitors provides the benefit of, for example, examining inhibition of a protein to a particular recognition site for a protein in order to nullify its influence on a given gene, as suggested by Church et al. (col. 23, lines 65-67), as would be useful for identifying compositions that are of potential scientific or clinical interest, as suggested by Church et al. (col. 28, lines 56-59).

As to claim 27 (dependent from claim 22), Applicant claims that the comparison is performed by a computer which classifies a profile into one of at least two subsets. This is not disclosed by Church et al. However, Church et al. do teach, with regard to forming the nucleic acid array, that while estimates of parameters may be made mentally, a computer may be used to assist in evaluation of parameters (col. 20, lines 31-35). Thus, Church et al. suggest in general that using a computer provides the

advantage of efficiency. Moreover, it has generally been recognized that the use of a conventional control to automate a previously manual operation involves only routine skill in the art . *In re Venner*, 120 USPQ 193 (CCPA 1958). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a computer to perform the step of comparison because Church et al. suggest that a computer provides the advantage of efficiency over performing a step mentally, and it has generally been recognized that the use of a conventional control, such as a computer in this case, to automate a previously manual operation involves only routine skill in the art.

3. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Church et al., 6,548,021, in view of Beutler et al., 5,234,811.

Church et al. disclose the invention substantially as claimed (see above with respect to claim 1). More specifically, Church et al. teach that an array of nucleic acid sequences immobilized on a support can be used for binding to proteins for which it has affinity and for subsequently eluting off the proteins in buffers of gradually increasing ionic strength to determine binding affinity, which is directly proportional to the salt concentration required to remove a given protein form a nucleic acid molecule (col. 23, lines 48-51). Church et al. thus teach that an array of double-stranded nucleic acid molecules (equivalent to the affinity molecules claimed by Applicant) is immobilized to the solid support before binding the protein. However, Church et al. do not teach an

embodiment wherein the nucleic acid is bound to the solid support *after* binding the complex.

However, Beutler et al. teach that probe/target hybrids may be selectively isolated on a solid matrix, such as hydroxylapatite, which preferentially binds double-stranded nucleic acids. Beutler et al. teach that this is an alternative to immobilizing probe nucleic acids on a solid support and using it to capture target sequences from solution (col. 14, lines 34-41). It would have been obvious to one of ordinary skill in the art at the time the invention was made to allow binding between the double stranded nucleic acid molecules to its target in the Church et al. invention before immobilizing the nucleic acid to a solid support because Beutler et al. teach that probe/target hybrids may be selectively isolated on a solid matrix, such as hydroxylapatite, which preferentially binds double-stranded nucleic acids and that this is an alternative to immobilizing probe nucleic acids on a solid support before capturing its target.

4. Claims 13 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Church et al., 6,548,021, in view of Hutchens et al., 5,719,060.

Church et al. disclose the invention substantially as claimed (see above with respect to claim 1). More specifically, Church et al. teach that an array of nucleic acid sequences immobilized on a support can be used for binding to proteins for which it has affinity and that the proteins may be identified by sequencing using standard methods, such as by mass spectrometry (e.g., liquid chromatography/electrospray ionization/ion trap tandem mass spectrometry) (see col. 23, lines 27-45). Church et al. teach that

following identification, the relative affinities of the double-stranded nucleic acid molecules for the proteins are assayed by binding the proteins to a solid support and eluting off the proteins in buffers of gradually increasing ionic strength to determine binding affinity, which is directly proportional to the salt concentration required to remove a given protein form a nucleic acid molecule (col. 23, lines 48-51). However, Church et al. do not teach that the solid support is a SELDI probe.

Hutchens et al. however teach a SELDI probe as a solid support for immobilization of affinity capture probes having specific affinity for an analyte and that the SELDI probe provides the advantages of providing much more efficient and sensitive affinity mass spectrometry (col. 11, lines 21-39 and col. 13, lines 40-60). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a SELDI probe as the solid support for the elution assay because Church et al. teach use of the solid supports in general for the elution washes and Hutchens et al. teach that a SELDI probe may be used to immobilize affinity capture probes having specific affinity for an analyte and that the SELDI probe provides the advantages of providing much more efficient and sensitive affinity mass spectrometry. One of ordinary skill in the art would recognize the advantages of using the SELDI probe as the solid support generally disclosed by Church et al. for mass spectrometry because of its efficiency and sensitivity. One of ordinary skill in the art would recognize that this solid support may also be used as the particular solid support disclosed by Church et al. for the elution washes to determine relative affinities between the nucleic acid and proteins because Church et al. teach use of a solid support in general for the

elution washes and give examples of a solid support, but does not limit the solid support to any particular type.

As to claim 20, Hutchens et al. teach that the SELDI (Surfaces Enhanced for Laser Desorption/Ionization) may be specifically SEND (Surfaces Enhanced for Neat Desorption), (col. 13, lines 40-44).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Ann Lam 6/12/06